

Remarks

After entry of the amendment, claims 162-238 are pending.

The specification has been amended to reflect the related applications.

Claims 1-161 have been canceled without prejudice. Claims 162-238 are supported by the specification and canceled claims 1-161.

No issues of new matter should arise and entry of the amendment is respectfully requested.

A. Anticipation Rejection

Claims 91, 99, 116, 119, 121, 122 and 124 are rejected under 35 USC § 102(b) as being anticipated by Boyer (US Patent No. 4,800,079).

Applicants respectfully traverse the rejection and respectfully submit that the claims are not anticipated by and are unobvious over Boyer for at least the following reasons: (1) the carrier particles are coated with an admixture comprising at least one hydrophilic polymer and micronized fenofibrate; and (2) the micronized fenofibrate is in admixture with the at least one hydrophilic polymer.

(1) Boyer teaches that the carrier particles are first coated with an alcohol solution containing methacrylic polymer (Boyer at column 2, lines 52-54). Thereafter, the fenofibrate particles are projected onto the methacrylic polymer that is adjacent to the carrier particles (Boyer at column 2, lines 55-58). Thus, the layer adjacent the carrier particles contains methacrylic polymer, but does not contain micronized fenofibrate.

In the claimed invention, the carrier particles are coated with an admixture of at least one hydrophilic polymer and micronized fenofibrate. Thus, the layer adjacent the carrier particles contains both hydrophilic polymer and micronized fenofibrate.

The claimed invention cannot be anticipated by Boyer because Boyer requires that a methacrylic polymer be coated on (e.g., adjacent to) the carrier particles, while the claims recite that a hydrophilic polymer and micronized fenofibrate are coated on (e.g., adjacent to) the carrier particles. In view thereof, Applicants respectfully request that the rejection under § 102 be withdrawn.

(2) Boyer teaches that the carrier particles are first coated with an alcohol solution containing methacrylic polymer (Boyer at column 2, lines 52-54). Thereafter, the fenofibrate particles are projected onto the methacrylic polymer that is coating the carrier particles (Boyer at

column 2, lines 55-58). The grains are immediately dried very rapidly to prevent the alcohol from dissolving the fenofibrate (Boyer at column 2, lines 64-67). Boyer teaches that a single thickness of microparticles is thus deposited on the sticky grain... (Boyer at column 3, lines 1-3). Boyer then teaches that the "operations of dampening-projecting-drying" can be repeated until all the powder has been incorporated (Boyer at column 3, lines 3-5).

In the claimed invention, the carrier particles are coated with an admixture of at least one hydrophilic polymer and micronized fenofibrate. "Admixture" is defined as "something that is produced by mixing." *The American Heritage® Dictionary of the English Language*, 4th Ed., (2000). "Admixture" is also defined as "the compound formed by mixing different substances together." *Webster's Revised Unabridged Dictionary* (1998). "Admixture" is also defined as "the act of mixing; 'paste made by a mixture of flour and water.'" *WordNet®*, Princeton University (1997). The dictionary definitions, obtained from www.dictionary.com, are attached hereto.

Applicants respectfully submit that Boyer's product (i.e., produced by providing a layer of polymer, then a layer of fenofibrate, then a layer of polymer, then a layer of fenofibrate, etc.) does not disclose or suggest the presently claimed admixture of at least one hydrophilic polymer and micronized fenofibrate. A product having alternating layers of different substances is not, by definition, a mixture of the substances. Accordingly, Boyer does not disclose or suggest the claimed admixture of hydrophilic polymer and fenofibrate. In view thereof, Applicants respectfully request that the rejection under § 102 be withdrawn.

B. Obviousness Rejection

Claims 92-98, 100-115, 117, 118, 120, 123 and 125-161 are rejected under 35 USC § 103 as being obvious over Boyer (US Patent No. 4,800,079) in view of Curtet et al (U.S. Patent No. 4,895,726).

Boyer does not provide any motivation or suggestion to produce a fenofibrate composition where the hydrophilic polymer is in admixture with micronized fenofibrate. In fact, Boyer teaches away from an admixture of polymer and micronized fenofibrate. At column 2, line 64 to column 3, line 3, Boyer teaches:

The grains are then immediately dried very rapidly in order to prevent the alcohol from having enough time to dissolve the fenofibrate.... This avoids destroying the microparticulate structure which offers a considerable area for encouraging absorption. A single thickness of microparticles is thus

deposited on the sticky grain where the microcapsules are fixed by adherence.

Boyer teaches that an admixture of hydrophilic polymer and micronized fenofibrate would result in the destruction of the microparticle structure of the fenofibrate. A reference that teaches away from a claimed invention cannot render it obvious.

Curtet does not cure the deficiencies in Boyer. One skilled in the art would not be motivated to combine Boyer and Curtet because Boyer teaches that the benefits of the invention are achieved by the methods of the invention which produce fenofibrate having a microparticle structure that is maintained by the manufacturing process described therein.

Curtet, however, teaches methods for preparing compositions containing fenofibrate and a solid surfactant by (i) intimately mixing and then co-micronizing the fenofibrate and the solid surfactant, (ii) adding lactose and starch to the mixture obtained, (iii) converting the whole to granules in the presence of water, (iv) drying the granules until they contain no more than 1% of water, (v) grading the granules, (vi) adding polyvinylpyrrolidone and magnesium stearate to the graded granules, and (vii) filling gelatin capsules with the mixture obtained in stage (vi). (Curtet at column 2, lines 5-20).

One skilled in the art would not be motivated by the teachings in Curtet to modify the process in Boyer in view of the fact that Boyer produces fenofibrate particles which maintain their microparticle structure and which are not mixed with a polymer.

In view of the above, Applicants respectfully submit that the presently claimed invention is unobvious over Boyer in view of Curtet.

In addition to the reasons discussed above, Applicants respectfully submit that the claimed invention produces unexpectedly superior results when compared to Boyer and Curtet. Applicants refer to the Declaration under 37 C.F.R. § 1.132 by Philippe Réginault (hereafter the Réginault Declaration) filed on July 8, 2003.

It is known in the art that the composition described by Boyer is represented by Lipanthyl® 250. *See* Réginault Declaration at ¶ 7. The composition recited in the claims is represented in the specification at Example 2 and by Lipanthyl® Supra. *See* Réginault Declaration at ¶ 8.

A comparison of the dissolution profile of Boyer (i.e., Lipanthyl® 250) and the claimed invention (i.e., Lipanthyl® Supra) is shown in Tables 1 and 2 and Figures 1 and 2 in the Réginault Declaration at ¶ 11.

For the Examiner's convenience, the results described in the Réginault Declaration and shown in Example 2 and Figure 1 in the present application are reproduced in the Table below.

Time	% Dissolution recited in Pending Claims	% Dissolution of Lipanthyl® 250 corresponding to Boyer	% Dissolution of Lipanthyl® Supra corresponding to the Invention	% Dissolution of Inventive Example 2 in the Application
5 minutes	at least 10%	0.4%	26.8%	18.9%
10 minutes	at least 20%	0.8%	60.5%	67.1%
20 minutes	at least 50%	1.2%	83.0%	89.7%
30 minutes	at least 75%	1.9%	89.8%	95.9%

In comparing Boyer and the claimed invention, the Réginault Declaration, at ¶ 12, states:

The results shown above clearly demonstrate that Lipanthyl® 250 (i.e., U.S. Patent No. 4,800,079 to Boyer) and Lipanthyl® Supra (i.e., the above-identified application) have very different dissolution profiles — both for the extent and for the rate. Lipanthyl® Supra presented a complete dissolution of fenofibrate within 1 hour whereas Lipanthyl® 250 only released 4% fenofibrate (i.e., 10 mg) within 1 hour. Hence, the two formulations have a significantly different dissolution profiles.

Based on the results shown in the Réginault Declaration and the specification at Example 2, Applicants respectfully submit that the presently claimed invention has an unexpectedly superior dissolution profile when compared to Boyer. Accordingly, Boyer does not render the claimed invention obvious, and one skilled in the art would not arrive at the presently claimed invention based on the teachings in Boyer.

Contrary to the assertion in the Advisory Action, the Declaration is commensurate in scope with the claims. Applicants respectfully submit that the critical differences between the claimed invention and Boyer are the structures of the products. Boyer is directed to a product having a layered structure (e.g., Lipanthyl® 250), while the claimed invention is directed to a product having an admixture comprising hydrophilic polymer and fenofibrate (e.g., Example 2 and Lipanthyl® Supra). The particle size and ratio of ingredients are not the critical distinction

between the claimed invention and Boyer. Accordingly, there is no reason to vary those parameters because the results shown in the Declaration would be the same. Again, criticality has been established because the Declaration shows that the claimed product having an admixture of hydrophilic polymer and fenofibrate has an unexpectedly superior dissolution profile when compared to Boyer, where the fenofibrate and polymer are layered with respect to each other.

Curtet does not cure the deficiencies of Boyer. Curtet corresponds to EP-A-0330532 which is discussed in detail in the specification at page 2, lines 1-20 and Examples 2-4. Curtet corresponds to Lipanthyl® 200M in Figures 1 and 2 in the present application.

The dissolution medium and conditions in the present claims are a rotating blade method at 75 rpm, where the dissolution medium is water with 2% polysorbate 80 or 0.025 M sodium lauryl sulfate. In contrast, Curtet uses a rotating vane or continuous flow cell where the dissolution medium is water with 0.1 M sodium lauryl sulfate. The dissolution medium of Curtet comprises much more sodium lauryl sulfate (i.e., a surfactant) than the dissolution medium of the invention. Having more surfactant will necessarily enhance dissolution. Accordingly, it is necessary to compare the composition described in the Curtet reference and the claimed composition using the same method. This was done in the instant application.

Applicants have shown in Example 2 of the application that the presently claimed invention has an unexpectedly superior dissolution profile compared to Lipanthyl® 200M (i.e., the teachings in Curtet). Example 2 and Figure 1 in the application demonstrate that the claimed composition has an unexpectedly superior dissolution profile when compared to Lipanthyl® 200M as described by Curtet. For the Examiner's convenience, a comparison of the dissolution profile recited in the present claims with the dissolution profile of Curtet (i.e., Lipanthyl® 200M) is shown in the Table below.

Time	% Dissolution Recited in Pending Claims	% Dissolution by Inventive Example shown in Example 2 of the Application	% Dissolution by Curtet as Lipanthyl® 200M shown in Example 2 of the Application
5 minutes	at least 10%	18.9%	0%
10 minutes	at least 20%	67.1%	3.7%
20 minutes	at least 50%	89.7%	31.2%
30 minutes	at least 75%	95.9%	54.9%

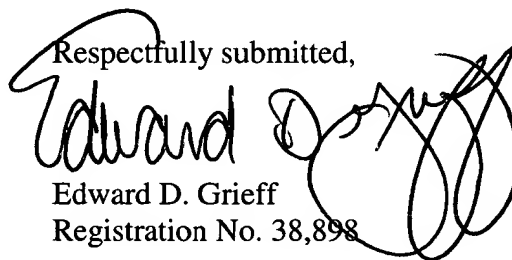
As shown from the summary above, Example 2 and Figure 1 in the application demonstrate that Curtet does not have a dissolution profile like the presently claimed dissolution profile.

Applicants respectfully submit that Curtet does not disclose or suggest a composition having the presently claimed dissolution profile, and that Curtet provides no motivation or suggestion to achieve the presently claimed dissolution profile.

In view of the above, Applicants respectfully submit that Boyer does not anticipate the presently claimed invention, and that Boyer in view of Curtet does not render the presently claimed invention obvious. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. §§ 102 and 103 be withdrawn.

An early and favorable reconsideration and allowance of claims 162-235 is respectfully requested. Examiner Sheikh is encouraged to contact the undersigned to expedite prosecution of this application.

Respectfully submitted,


Edward D. Grieff
Registration No. 38,898

Date: September 8, 2003

HALE AND DORR LLP
1455 Pennsylvania Avenue, NW
Washington, DC 20004
Phone: 202-942-8400